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TOWNSEND and TOWNSEND and CREW LLP

By: Sylvia E. Arnold

Sylvia E. Arnold

PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:	Confirmation No. 5304
Steven R. Binder	Examiner: Pablo S. Whaley
Application No.: 10/828,846	Technology Center/Art Unit: 1631
Filed: April 20, 2004	APPEAL BRIEF UNDER 37 CFR §1.192
For: PATTERN RECOGNITION METHOD FOR DIAGNOSIS OF SYSTEMIC AUTOIMMUNE DISEASES	
Customer No.: 20350	

Mail Stop Appeal Brief
Commissioner for Patents
Board of Patent Appeals and Interferences
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellant hereby submits this appeal brief pursuant to 37 CFR §1.192(a). An Electronic Acknowledgement Receipt generated upon the submission of the Notice of Appeal indicates that the date of receipt of appellant's notice of appeal is June 30, 2010. Thus, pursuant to 37 CFR §1.192(a), this Appeal Brief was due on August 30, 2010, extensions of time being permitted. Accordingly, Appellants request a two month extension of time to extend the due date to October 30, 2010. The Commissioner is hereby authorized to charge deposit account no. 20-1430.

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REAL PARTY IN INTEREST:

The real party in interest of the subject patent application is Bio-Rad Laboratories, Inc., the owner of the patent application.

RELATED APPEALS AND INTERFERENCES:

Appellant is aware of one related appeal. The appeal and decision from the parent application 09/691,405, are provided in the Related Proceedings Appendix.

There are no other known related appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS:

Claims 1-33 are pending. Claims 1-33 stand rejected. Appellants appeal from the rejections of claims 1-33.

STATUS OF AMENDMENTS:

No amendments have been filed subsequent to receipt of the final Office Action mailed on December 31, 2009, which has necessitated this Appeal.

SUMMARY OF THE CLAIMED SUBJECT MATTER:

The present disclosure teaches a system for identifying whether the antibody profile of a patient test sample corresponds with particular systemic autoimmune diseases (SADs) from a set of SADs sought to be investigated for the patient. The training set with which a test sample is compared includes data associated with the SADs sought to be investigated for a particular patient or patients. The training set is made up of reference samples that have disease conditions that are known as well as samples that are known to be disease free ("none"). Each reference sample may therefore be associated with, none, one or more of the systemic autoimmune diseases. When the test sample data set is statistically compared with the training data set using a nearest neighbor process, or algorithm, such as a k-nearest neighbor (KNN) process, or algorithm, a determination of one or more particular diseases may be achieved. Where a determination of more than one disease is made, the diseases are considered equally likely to be present in the patient test sample. This condition is known as "overlap syndrome."

The present invention provides a computer-implemented method of identifying whether a test subject is suffering from one or more SADs. The present invention may be implemented with the aid of computer software in a computer based system such as a medical decision support system. (See, e.g., paragraph [0019])

In one embodiment, for example as recited in claim 1, the present invention provides a computer-implemented method of identifying whether a patient test sample is associated with one or more of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample. This method typically includes storing a plurality of reference data sets in a memory (see, e.g., paragraph [0024] and [0025] and p. 10, lines 16-18), each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies (see, e.g., p. 8, lines 10-15), wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD (see, e.g., p. 8, lines 5-9), and wherein said reference data sets include at least one

reference data set associated with none of the specific SADs (see, e.g., 8, lines 5-9). This method also typically includes receiving, in a computer system, a sample data set having quantitative values representing levels for each of said plurality of autoantibodies for a patient test sample (see, e.g., paragraph [0026]), and automatically applying, in the computer system, a k-nearest neighbor process (see, e.g., paragraph [0027], [0029] and [0030] generally, and also paragraphs [0032] through [0038]] for a specific embodiment and examples]) to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs (see, e.g., p. 10, lines 23-28, and paragraph [0048]). This method also typically includes providing the statistically derived decision as output (see, e.g., paragraph [0032]), the decision identifying which one or more of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases.

Another embodiment, as recited in claim 18, provides a computer system configured to provide output data indicating whether a patient test sample is associated with one or more of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample (see, e.g., paragraphs [0019] through [0023] generally]). The computer system typically includes a memory module that stores a plurality of reference data sets (see, e.g., p. 5, lines 29-30; p.6, lines 2-3), each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the specific SADs (see, e.g., p. 10, lines 16 - 18; p. 8, lines 5-15). The system also typically includes a means for receiving a sample data set having quantitative

values representing levels for each of said plurality of autoantibodies for a patient test sample (see, e.g., p. 5, line 30 – p. 6, line 2; p. 6, lines 9-20). The system also typically includes a processor (see e.g., 5, lines 29-30; p. 7, lines 9-31; p. 11, lines 9-10) configured to analyze the sample data set and the reference data sets by applying a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with none, one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs (see, e.g., p. 10, lines 23-28, and paragraph [0048]). This system also typically includes a means for providing output data (see, e.g., p. 6, line 4; paragraphs [0021] and [0032]) including the statistically derived decision, the decision identifying which one or more of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases.

Another embodiment, as recited in claim 32 provides a computer-implemented method of identifying whether a patient test sample is equally likely to be associated with more than one of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample. This method typically includes storing a plurality of reference data sets in a memory (see, e.g., paragraph [0024] and [0025] and p. 10, lines 16-18), each reference data set having values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD (see, e.g., p. 8, lines 5-9), and wherein said reference data sets include at least one reference data set associated with none of the specific SADs (see, e.g., p. 8, lines 5-9). This method also typically includes receiving, in a computer system, a sample data set having values representing levels for each of said plurality of autoantibodies for a patient test sample (see, e.g., paragraph [0026]), and automatically applying, in the computer system, a k-nearest neighbor process (see, e.g., paragraph [0027], [0029] and

[0030] generally, and also paragraphs [0032] through [0038]] for a specific embodiment and examples]) to the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with more than one of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs (see, e.g., p. 10, lines 23-28, and paragraph [0048]). The method also typically includes providing the statistically derived decision as output (see, e.g., paragraph [0032]), the decision identifying which of the more than one of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with more than one of said systemic autoimmune diseases.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL:

The issues on appeal are:

Whether claims 1, 6, 10-18 and 22-33 are unpatentable under 35 U.S.C. §103(a) over Zimmerman et al. (Electrophoresis, 1995, Vol. 16, p. 941-947), in view of Cabello et al. (Int. J. Biomed. Comput., 1991, Vol. 27, p.77-93), and in view of Kanai (U.S. 5,619,990).

Whether claims 2-5 and 19-22 are unpatentable under 35 U.S.C. §103(a) over Zimmerman et al., in view of Cabello et al., and in view of Kanai, and further in view of Osterland (Clinical Chemistry, 1994, Vol. 40, No. 11(B), p.2146-2153).

Whether claims 7, 8 and 9 are unpatentable under 35 U.S.C. §103(a) over Zimmerman et al., in view of Cabello et al., in view of Kanai et al., and in view of Osterland, and further in view of Kopecky (Design and Implementation of the Internet-Based Medical Expert System ToxoNet, 1999, p. 1-153).

ARGUMENT

I. Rejection under 35 USC §103(a) over Zimmerman et al., in view of Cabello et al., in view of Kanai.

Claim 32

Brief Recap of Main Cited References

Zimmerman analyzes Western blots using neural network pattern recognition analysis techniques.

Cabello teaches fuzzy k-nearest neighbor classifiers for classification of sample data to one of a plurality of different disease classes. Cabello teaches selection of a single disease (see, e.g., p 89, first full paragraph: "...thus, we consider as the membership degree the largest of them.")

Kanai teaches a system that provides a medical diagnosis by discriminating attribution degrees. Kanai teaches determining the most probable disease to which a test data group is associated from multiple diseases using a ranking program, wherein the output is a ranked output of mutually exclusive diseases (see e.g., col. 5, lines 41-47; and FIG 10).

Arguments

Applicants respectfully assert that the cited references, taken alone or in combination as suggested in the last Office Action, fail to teach or suggest limitations of the claims. For example, the cited references fail to teach or suggest "automatically applying, in the computer system, a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets **to produce a statistically derived decision indicating whether**, out of a range of none, one and more than one of said systemic autoimmune diseases, **the patient test sample is associated with more than one of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs,**" and "providing the statistically derived decision as output, the **decision identifying which of the more than one of said systemic autoimmune diseases the patient**

test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases" as is recited in claim 32 (emphasis added).

One outcome of a k-nearest neighbor process applied to the data as recited in claim 32 is that the patient test sample will be found to be clear of the systemic autoimmune diseases (SADs). Another outcome is that the patient test sample will be found to have one of the SADs. Another possible outcome is that the patient test sample will be found to have more than one of the SADs, where each of the diseases are considered as equally likely to be present in the patient test sample. This is significant because many people do, in fact, fit the definition of having more than one disease or have what is called "overlap syndrome", which is a condition where there are symptoms consistent with more than one disease and where the patient may actually suffers from those diseases. The cited references, taken individually or in combination, fail to teach or suggest the capacity to provide a statistically derived decision that identifies more than one SAD that the patient test sample is considered equally likely to have. For example, neural network analysis as taught by Zimmerman would at best provide a statistical determination of a single disease. The techniques taught by Cabello teach outputting a single top candidate, and the techniques of Kanai teach determining to which of a plurality of **mutually exclusive disease groups** a patient most likely belongs. Thus, there is a difference between the claimed invention as recited in claim 32 and a combination of the cited references in that there is a capacity to quantitatively determine and identify more than one of the SADs wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have the identified SADs. Again, the cited references lack this capacity. One technical effect of this difference is that a much more complete diagnosis of a patient sample may be performed using the presently claimed invention. For example, a patient sample found to have more than one of the SADs will alert a physician to the overlap syndrome condition so that further investigations can be made looking for more than one of the SADs as the decision indicates that they are equally likely to be in the patient test sample.

Applicants also would like to point out that one skilled in the art would not look to Kanai for the purposes of the presently claimed invention as Kanai is not relevant to finding any type of overlap condition, e.g., two equally likely diseases. This is clear from Kanai at page 79:

> "However, there will be regions where the properties of the data vectors of the different classes will show considerable overlap in the measurement space. By means of the fuzzy description of the learning set, we try to get the labels of the data vectors to reflect more precisely the relation between their properties. Consequently, if the assignation of labels is adequate, the errors of the classifier will be lower."

This passage follows with the purpose of Kanai, which is to discriminate between mutually exclusive arythmias and identify a particular arythmia using classifiers. By reducing errors in the classifiers, Kanai purposely removes overlap of mutually exclusive disease types so as to discriminate between mutually exclusive arythmias (e.g., it is not possible for a patient to be suffering from more than one of the arythmias). Hence, one skilled in the art would not look to Kanai when considering a system or method having the ability to identify equally likely systemic autoimmune diseases. The purpose of the invention recited in claim 32, on the other hand, is to provide a statistically derived decision "identifying which of the more than one of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with more than one of said systemic autoimmune diseases." The cited references when combined do not provide the ability to identify the more than one equally likely SADs the patient test sample is associated with.

Accordingly, Applicants respectfully request withdrawal of the rejections to claim 32 for at least the above reasoning.

Claims 1-31, 33

Applicants respectfully assert that the cited references, taken alone or in combination as suggested in the last Office Action, fail to teach or suggest limitations of the claims. For example, the cited references fail to teach or suggest "automatically applying, in the

computer system, a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs" as is recited in claim 1 (emphasis added). Similar limitations are presented in independent claim 18.

One outcome of a k-nearest neighbor process applied to the data as recited in the claims is that the patient test sample will be found to be clear of the systemic autoimmune diseases (SADs). Another outcome is that the patient test sample will be found to have one of the SADs. Another possible outcome is that the patient test sample will be found to have more than one of the SADs, where each of the diseases are considered as equally likely to be present in the patient test sample. This is significant because many people do, in fact, fit the definition of having more than one disease or have what is called "overlap syndrome", which is a condition where there are symptoms consistent with more than one disease. The cited references, taken individually or in combination, fail to teach or suggest the capacity to provide a statistically derived decision where the outcome indicates which of one or more of the SADs the patient test sample is associated, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have the identified SADs. For example, neural network analysis as taught by Zimmerman, would at best provide a single disease as output. The techniques taught by Cabello teach outputting a single top candidate. The techniques of Kanai teach determining to which of a plurality of mutually exclusive disease groups a patient most likely belongs. As above, Kanai discriminates between mutually exclusive arythmias and identifies a particular arythmia using classifiers. Thus, there is a difference between the claimed invention as recited in claim 1 (and 18) and a combination of the cited references in that there is a capacity to quantitatively determine and identify one or more of the SADs and if the decision identifies more than one SAD, the patient test sample is considered equally likely to have the identified SADs. The cited references lack this capacity. One technical effect of this difference

is that a much more complete diagnosis of a patient sample may be performed using the presently claimed invention. For example, a patient sample may be found to have more than one of the SADs in which case further investigations can be made looking for more than one of the SADs as the decision indicates that they are equally likely to be in the patient test sample.

It is respectfully submitted that the remaining cited references, Osterland and Kopecky, fail to remedy the deficiencies of Zimmerman, Cabello and Kanai as discussed above. Accordingly, Applicants respectfully request withdrawal of the rejections to claim 1 and 18 for at least the above reasoning. Further, Applicants respectfully request withdrawal of the rejections to the dependent claims, based at least on their dependency to claims 1 and 18.

Respectfully submitted,

Gerald T. Gray
Reg. No. 41,797

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
GTG:sea
62863222 v1

CLAIMS APPENDIX

1. (Previously Presented) A computer-implemented method of identifying whether a patient test sample is associated with one or more of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample; the method comprising:

storing a plurality of reference data sets in a memory, each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the specific SADs;

receiving, in a computer system, a sample data set having quantitative values representing levels for each of said plurality of autoantibodies for a patient test sample; and

automatically applying, in the computer system, a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs; and

providing the statistically derived decision as output, the decision identifying which one or more of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases.

2. (Original) The computer-implemented method of claim 1, wherein the SADs include two or more systemic autoimmune diseases selected from the group consisting of systemic lupus erythmatosus, scleroderma (SLE), Sjögren's syndrome (SS), polymyositis (PMYO), dermatomyositis (DMYO), CREST, and mixed connective tissue disease (MCTD).

3. (Original) The computer-implemented method of claim 1, wherein the SADs include two or more systemic autoimmune diseases selected from the group consisting of systemic lupus erythmatosus (SLE), scleroderma, Sjögren's syndrome (SS), myositis (MYO), polymyositis (PMYO), dermatomyositis (DMYO), CREST, connective tissue disease (CTD), fibromyalgia, osteroarthritis (OA), Reynaud's syndrome and Rheumatoid arthritis (RA).

4. (Original) The computer-implemented method of claim 1, wherein said plurality of autoantibodies comprises antibodies to at least ten of the following antigens:

SSA 60,
SSA 52,
SSB 48,
Sm BB',
Sm D1,
Sm,
SmRNP
RNP 68,
RNP A,
RNP C,
Fibrillarin,
Riboproteins P0, P1, and P2,
dsDNA,
Nucleosome,
Ku,
Centromere A,
Centromere B,
Scl-70,
Pm-Scl,
RNA-Polymerases 1, 2, and 3,

Th,
Jo-1,
Mi-2,
PL7,
PL12, and
SRP.

5. (Original) The computer-implemented method of claim 1, wherein said plurality of autoantibodies consists of antibodies to the following antigens:

SSA 60,
SSA 52,
SSB 48,
Sm,
SmRNP,
RNP 68,
RNP A,
Riboproteins P0, P1, and P2,
dsDNA,
Nucleosome,
Centromere B,
Scl-70, and
Jo-1.

6. (Previously Presented) The computer-implemented method of claim 1, wherein providing includes generating a display output including said indication of whether the patient test sample is associated with none, one or more of the specific SADs.

7. (Original) The computer-implemented method of claim 6, wherein generating includes transmitting display output data to a remote computer system and rendering the display output on a display screen coupled with the remote computer system.

8. (Original) The computer-implemented method of claim 1, wherein receiving includes receiving the sample data set from an automated test system over a network connection.

9. (Original) The computer-implemented method of claim 8, wherein storing includes receiving the reference data sets from the automated test system over the network connection.

10. (Original) The computer-implemented method of claim 1, wherein storing includes receiving the reference data sets from one or more test sources.

11. (Original) The computer-implemented method of claim 1, wherein the k-nearest neighbor process includes determining, for each of the reference data sets, a concordance value between the sample data set and the reference data set, and comparing each concordance value to a threshold value, wherein only a first plurality of the reference data sets having a concordance value that exceeds the threshold value are used by the process.

12. (Original) The computer-implemented method of claim 11, wherein the k-nearest neighbor process further includes determining, for each of the reference data sets, a distance metric value between the sample data set and the reference data set.

13. (Original) The computer-implemented method of claim 11, wherein the process further includes:

determining whether the number of the first plurality of reference data sets exceeds a minimum cutoff value, and

if not, providing an indication that the patient test sample is associated with none of the specific SADs, and

if so, determining whether the patient test sample is associated with one or more of the specific SADs.

14. (Original) The computer-implemented method of claim 11, wherein the process further includes determining a disease concordance value for each of the first plurality of reference data sets.

15. (Original) The computer-implemented method of claim 14, wherein determining a disease concordance value includes:

for each SAD associated with the first plurality of reference data sets:

adding the number of the first plurality of reference data sets associated with that SAD and dividing by the total number of the first plurality of reference data sets to produce a disease concordance value for that SAD.

16. (Original) The computer-implemented method of claim 15, further including comparing each disease concordance value with a first threshold value, and returning the SAD associated with the concordance value that exceeds the first threshold value.

17. (Original) The computer-implemented method of claim 16, further including comparing each disease concordance value with a second threshold value, and returning the SAD associated with the concordance value that exceeds the second threshold value.

18. (Previously Presented) A computer system configured to provide output data indicating whether a patient test sample is associated with one or more of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample; the system comprising:

a memory module that stores a plurality of reference data sets, each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the specific SADs;

a means for receiving a sample data set having quantitative values representing levels for each of said plurality of autoantibodies for a patient test sample;

a processor configured to analyze the sample data set and the reference data sets by applying a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with none, one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs; and

a means for providing output data including the statistically derived decision, the decision identifying which one or more of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases.

19. (Original) The system of claim 18, wherein the SADs include two or more systemic autoimmune diseases selected from the group consisting of systemic lupus erythmatosus (SLE), scleroderma, Sjögren's syndrome (SS), myositis (MYO), polymyositis (PMYO), dermatomyositis (DMYO), CREST, connective tissue disease (CTD), fibromyalgia, osteroarthritis (OA), Reynaud's syndrome and Rheumatoid arthritis (RA).

20. (Original) The system of claim 18, wherein said plurality of autoantibodies comprises antibodies to at least ten of the following antigens:

SSA 60,

SSA 52,

SSB 48,
Sm BB',
Sm D1,
Sm,
SmRNP,
RNP 68,
RNP A,
RNP C,
Fibrillarin,
Riboproteins P0, P1, and P2,
dsDNA,
Nucleosome,
Ku,
Centromere A,
Centromere B,
Scl-70,
Pm-Scl,
RNA-Polymerases 1, 2, and 3,
Th,
Jo-1,
Mi-2,
PL7,
PL12, and
SRP.

21. (Original) The system of claim 18, wherein said plurality of autoantibodies consists of antibodies to the following antigens:

SSA 60,

SSA 52,
SSB 48,
Sm,
SmRNP,
RNP 68,
RNP A,
Riboproteins P0, P1, and P2,
dsDNA,
Nucleosome,
Centromere B,
Scl-70, and
Jo-1.

22. (Original) The system of claim 18, wherein the means for providing the output data includes one of a monitor for displaying the output data, a printer for printing the output data and a communication interface device for providing the output data to a separate computer system.

23. (Original) The system of claim 18, wherein the means for receiving the sample data set includes one of an interface device configured to receive data from a remote automated test system, a manual input device, and a device configured to read data from a computer readable medium.

24. (Previously Presented) The system of claim 18, wherein the memory module includes one of a RAM, a ROM, a computer readable disk medium, a hard disk drive and a separate database system.

25. (Original) The system of claim 18, wherein the k-nearest neighbor process determines, for each of the reference data sets, a concordance value between the sample data set and the reference data set, and compares each concordance value to a threshold value,

wherein only a first plurality of the reference data sets having a concordance value that exceeds the threshold value are used by the process.

26. (Original) The system of claim 25, wherein the k-nearest neighbor process further determines, for each of the reference data sets, a distance metric value between the sample data set and the reference data set.

27. (Original) The system of claim 25, wherein the k-nearest neighbor process further determines whether the number of the first plurality of reference data sets exceeds a minimum cutoff value, and

if not, provides an indication that the patient test sample is associated with none of the specific SADs, and

if so, determines whether the patient test sample is associated with one or more of the specific SADs.

28. (Original) The system of claim 25, wherein the k-nearest neighbor process further determines a disease concordance value for each of the first plurality of reference data sets.

29. (Original) The system of claim 28, wherein a disease concordance value is determined for each SAD associated with the first plurality of reference data sets by adding the number of the first plurality of reference data sets associated with that SAD and dividing by the total number of the first plurality of reference data sets to produce a disease concordance value for that SAD.

30. (Original) The system of claim 29, wherein the process further compares each disease concordance value with a first threshold value, and returns the SAD associated with the concordance value that exceeds the first threshold value.

31. (Original) The system of claim 30, wherein the process further compares each disease concordance value with a second threshold value, and returns the SAD associated with the concordance value that exceeds the second threshold value.

32. (Previously Presented) A computer-implemented method of identifying whether a patient test sample is equally likely to be associated with more than one of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample; the method comprising:

storing a plurality of reference data sets in a memory, each reference data set having values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the specific SADs;

receiving, in a computer system, a sample data set having values representing levels for each of said plurality of autoantibodies for a patient test sample; and

automatically applying, in the computer system, a k-nearest neighbor process to the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with more than one of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs; and

providing the statistically derived decision as output, the decision identifying which of the more than one of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with more than one of said systemic autoimmune diseases.

33. (Previously Presented) A computer-implemented method of identifying whether a patient test sample is associated with one or more of a plurality of specific systemic

autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample; the method comprising:

storing a plurality of reference data sets in a memory, each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the specific SADs;

receiving, in a computer system, a sample data set having quantitative values representing levels for each of said plurality of autoantibodies for a patient test sample; and

automatically applying, in the computer system, a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a non-ranked statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs; and

providing the statistically derived decision as output, the decision identifying which one or more of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases.

EVIDENCE APPENDIX

none

RELATED PROCEEDINGS APPENDIX

Attached are the following documents from parent application Serial No. 09/691,405:

Appeal Brief Under 37 CFR §§41.31 and 41.37 filed November 13, 2006;

Supplemental Appeal Brief Under 37 CFR §§41.31 and 41/37 filed December 28, 2006; and

Office Action dated April 30, 2007.